

### AMENDMENTS TO THE CLAIMS

The following listing of claims will replace all prior versions, and listings, of claims in the application.

#### Listing of claims:

**Claim 1 (currently amended).** A compound of Formula I



or a pharmaceutically acceptable salt thereof,

wherein:

Z is selected from:

HO<sub>2</sub>C;

HO(H)N(O)C;

H(O)C-N(OH);

CH<sub>3</sub>(O)C-N(OH);

CH<sub>3</sub>(H)N(O)C-N(OH);

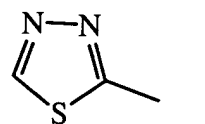
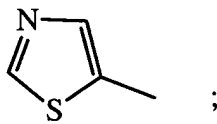
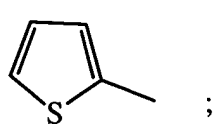
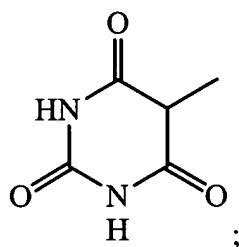
HS;

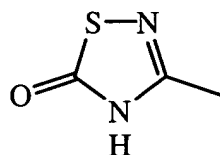
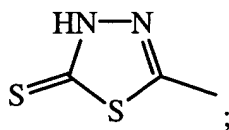
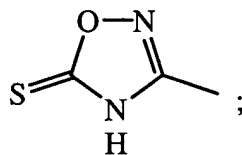
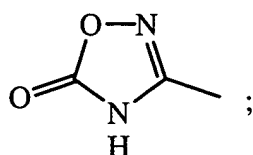
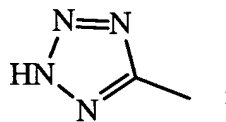
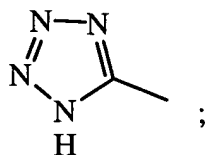
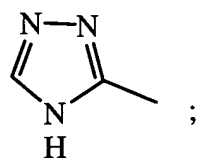
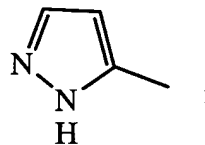
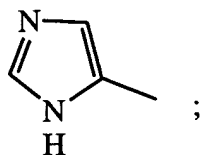
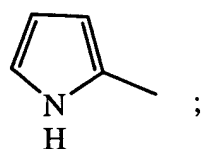
H<sub>2</sub>N(O)<sub>2</sub>S;

CH<sub>3</sub>(H)N(O)<sub>2</sub>S;

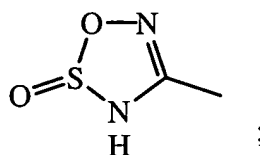
HO(O)P;

(HO)<sub>2</sub>(O)P;





; and



L is selected from:

$C_3$ - $C_5$  alkylenyl;

Substituted  $C_3$ - $C_5$  alkylenyl;

3- to 5-membered heteroalkylenyl; and

Substituted 3- to 5-membered heteroalkylenyl;

Substituted L groups contain 1 or 2 substituents on a carbon atom or nitrogen atom independently selected from:

HO;

CN; and

CF<sub>3</sub>;

wherein each substituent on a carbon atom may further be independently F, and wherein 2 substituents may be taken together with a carbon atom to which they are both bonded to form the group C=O;

R<sup>1</sup> is independently selected from:

C<sub>5</sub> or C<sub>6</sub> cycloalkylenyl-(C<sub>1</sub>-C<sub>8</sub> alkylenyl);  
Substituted C<sub>5</sub> or C<sub>6</sub> cycloalkylenyl-(C<sub>1</sub>-C<sub>8</sub> alkylenyl);  
5- or 6-membered heterocycloalkylenyl-(C<sub>1</sub>-C<sub>8</sub> alkylenyl);  
Substituted 5- or 6-membered heterocycloalkylenyl-(C<sub>1</sub>-C<sub>8</sub> alkylenyl);  
Phenylenyl-(C<sub>1</sub>-C<sub>8</sub> alkylenyl);  
Substituted phenylenyl-(C<sub>1</sub>-C<sub>8</sub> alkylenyl);  
5- or 6-membered heteroarylenyl-(C<sub>1</sub>-C<sub>8</sub> alkylenyl);  
Substituted 5- or 6-membered heteroarylenyl-(C<sub>1</sub>-C<sub>8</sub> alkylenyl);  
Phenyl;  
Substituted phenyl;  
Naphthyl;  
Substituted naphthyl;  
5- or 6-membered heteroaryl;  
Substituted 5- or 6-membered heteroaryl;  
8- to 10-membered heterobiaryl; and  
Substituted 8- to 10-membered heterobiaryl;

R<sup>2</sup> is independently selected from:

H;  
C<sub>1</sub>-C<sub>6</sub> alkyl;  
Phenyl-(C<sub>1</sub>-C<sub>8</sub> alkylenyl);  
Substituted phenyl-(C<sub>1</sub>-C<sub>8</sub> alkylenyl);  
Naphthyl-(C<sub>1</sub>-C<sub>8</sub> alkylenyl);  
Substituted naphthyl-(C<sub>1</sub>-C<sub>8</sub> alkylenyl);  
5- or 6-membered heteroaryl-(C<sub>1</sub>-C<sub>8</sub> alkylenyl);  
Substituted 5- or 6-membered heteroaryl-(C<sub>1</sub>-C<sub>8</sub> alkylenyl);  
8- to 10-membered heterobiaryl-(C<sub>1</sub>-C<sub>8</sub> alkylenyl);  
Substituted 8- to 10-membered heterobiaryl-(C<sub>1</sub>-C<sub>8</sub> alkylenyl);  
Phenyl-O-(C<sub>1</sub>-C<sub>8</sub> alkylenyl);  
Substituted phenyl-O-(C<sub>1</sub>-C<sub>8</sub> alkylenyl);  
Phenyl-S-(C<sub>1</sub>-C<sub>8</sub> alkylenyl);

Substituted phenyl-S-(C<sub>1</sub>-C<sub>8</sub> alkylene);

Phenyl-S(O)-(C<sub>1</sub>-C<sub>8</sub> alkylene);

Substituted phenyl-S(O)-(C<sub>1</sub>-C<sub>8</sub> alkylene);

Phenyl-S(O)<sub>2</sub>-(C<sub>1</sub>-C<sub>8</sub> alkylene); and

Substituted phenyl-S(O)<sub>2</sub>-(C<sub>1</sub>-C<sub>8</sub> alkylene);

Each substituted R<sup>1</sup> group contains from 1 to 3 substituents, and each substituted R<sup>2</sup> group contains from 1 to 4 substituents, wherein each substituent is independently on a carbon or nitrogen atom, independently selected from:

C<sub>1</sub>-C<sub>6</sub> alkyl;

CN;

CF<sub>3</sub>;

HO;

(C<sub>1</sub>-C<sub>6</sub> alkyl)-O;

(C<sub>1</sub>-C<sub>6</sub> alkyl)-S(O)<sub>2</sub>;

H<sub>2</sub>N;

(C<sub>1</sub>-C<sub>6</sub> alkyl)-N(H);

(C<sub>1</sub>-C<sub>6</sub> alkyl)<sub>2</sub>-N;

(C<sub>1</sub>-C<sub>6</sub> alkyl)-C(O)O-(C<sub>1</sub>-C<sub>8</sub> alkylene)<sub>m</sub>;

(C<sub>1</sub>-C<sub>6</sub> alkyl)-C(O)O-(1- to 8-membered heteroalkylene)<sub>m</sub>;

(C<sub>1</sub>-C<sub>6</sub> alkyl)-C(O)N(H)-(C<sub>1</sub>-C<sub>8</sub> alkylene)<sub>m</sub>;

(C<sub>1</sub>-C<sub>6</sub> alkyl)-C(O)N(H)-(1- to 8-membered heteroalkylene)<sub>m</sub>;

H<sub>2</sub>NS(O)<sub>2</sub>-(C<sub>1</sub>-C<sub>8</sub> alkylene);

(C<sub>1</sub>-C<sub>6</sub> alkyl)-N(H)S(O)<sub>2</sub>-(C<sub>1</sub>-C<sub>8</sub> alkylene)<sub>m</sub>;

(C<sub>1</sub>-C<sub>6</sub> alkyl)<sub>2</sub>-NS(O)<sub>2</sub>-(C<sub>1</sub>-C<sub>8</sub> alkylene)<sub>m</sub>;

3- to 6-membered heterocycloalkyl-(G)<sub>m</sub>;

Substituted 3- to 6-membered heterocycloalkyl-(G)<sub>m</sub>;

5- or 6-membered heteroaryl-(G)<sub>m</sub>;

Substituted 5- or 6-membered heteroaryl-(G)<sub>m</sub>;

(C<sub>1</sub>-C<sub>6</sub> alkyl)-S(O)<sub>2</sub>-N(H)-C(O)-(C<sub>1</sub>-C<sub>8</sub> alkylene)<sub>m</sub>; and

(C<sub>1</sub>-C<sub>6</sub> alkyl)-C(O)-N(H)-S(O)<sub>2</sub>-(C<sub>1</sub>-C<sub>8</sub> alkylene)<sub>m</sub>;

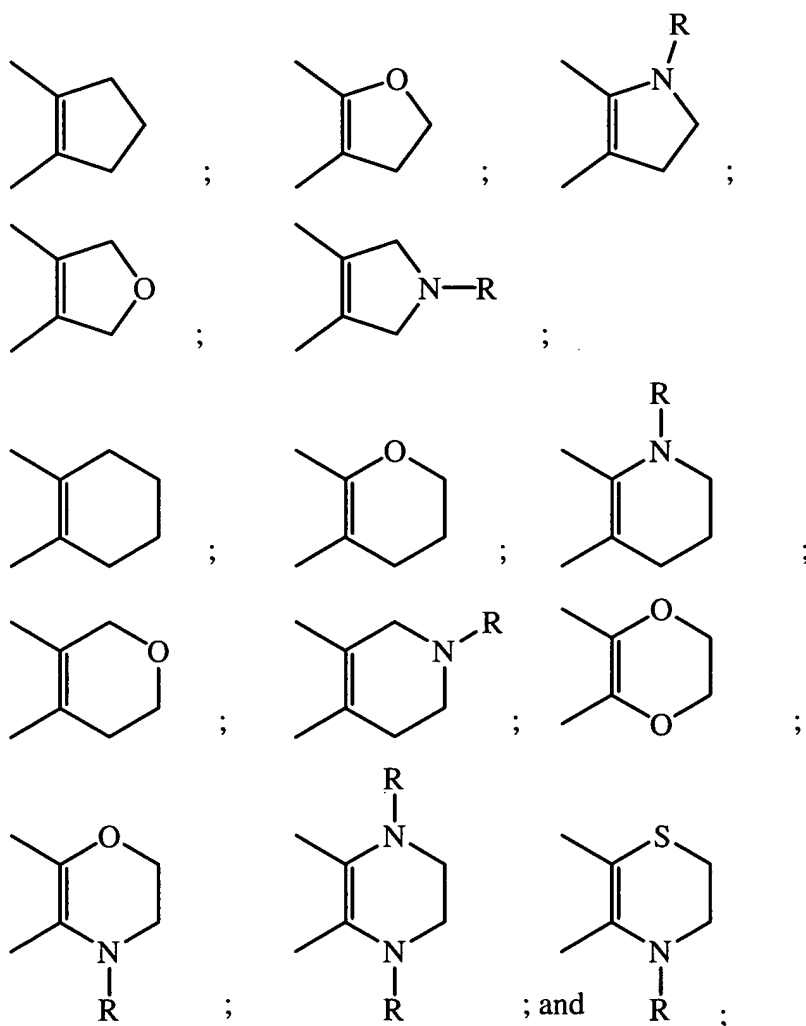
wherein each substituent on a carbon atom may further be independently selected from:

Halo; and

HO<sub>2</sub>C;

wherein 2 substituents may be taken together with a carbon atom to which they are both bonded to form the group C=O;

wherein two adjacent, substantially sp<sup>2</sup> carbon atoms may be taken together with a diradical substituent to form a cyclic diradical selected from:



R is H or C<sub>1</sub>-C<sub>6</sub> alkyl;

G is CH<sub>2</sub>; O, S, S(O); or S(O)<sub>2</sub>;

Each m is an integer of 0 or 1;

Q, when bonded to a nitrogen atom in group D, is selected from:

OC(O);

CH(R<sup>6</sup>)C(O);

OC(NR<sup>6</sup>);

CH(R<sup>6</sup>)C(NR<sup>6</sup>);

N(R<sup>6</sup>)C(O);

N(R<sup>6</sup>)C(S);

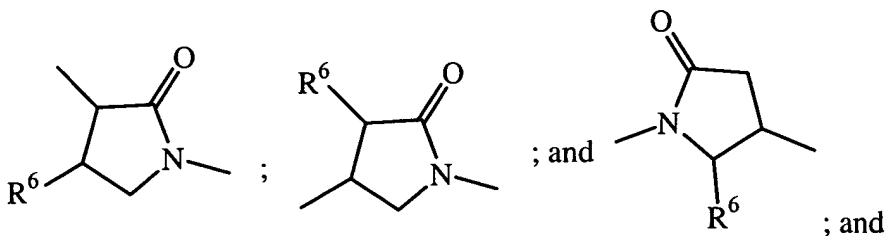
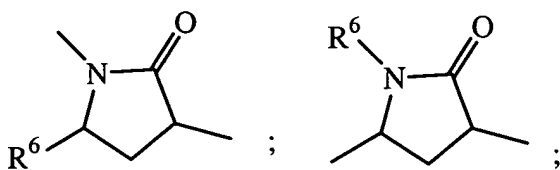
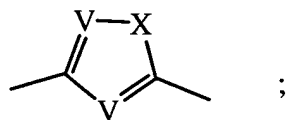
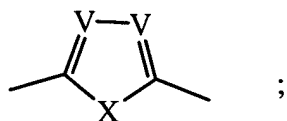
N(R<sup>6</sup>)C(NR<sup>6</sup>);

SC(O);

CH(R<sup>6</sup>)C(S);

SC(NR<sup>6</sup>);

C≡CCH<sub>2</sub>;



Q, when bonded to a carbon atom in group D, is as defined above and may further be selected from:

OCH<sub>2</sub>;

N(R<sup>6</sup>)CH<sub>2</sub>;

trans-(H)C=C(H);

cis-(H)C=C(H);

C≡C;

CH<sub>2</sub>C≡C;

CF<sub>2</sub>C≡C;

C≡CCF<sub>2</sub>;

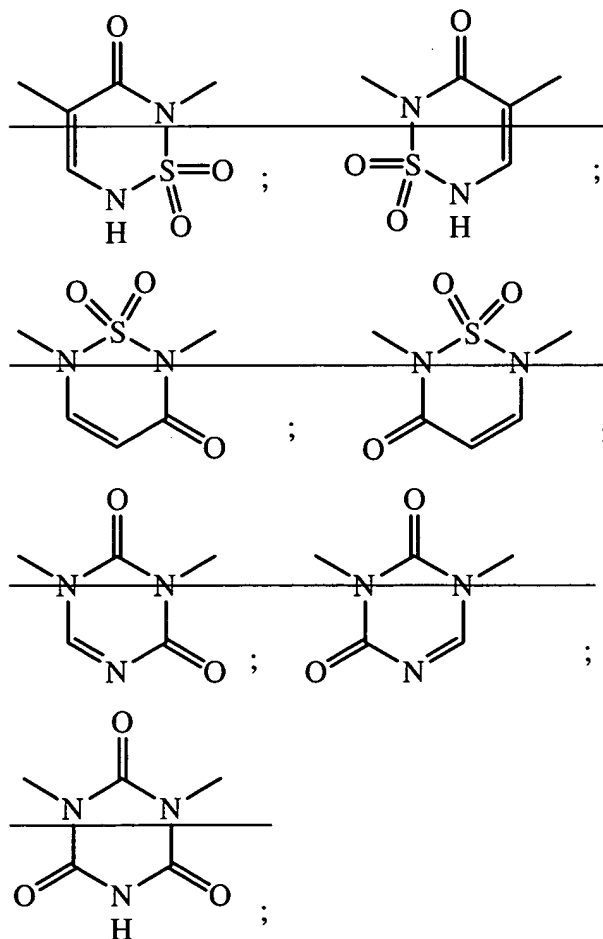
Each R<sup>6</sup> independently is H, C<sub>1</sub>-C<sub>6</sub> alkyl, C<sub>3</sub>-C<sub>6</sub> cycloalkyl; 3- to 6-membered

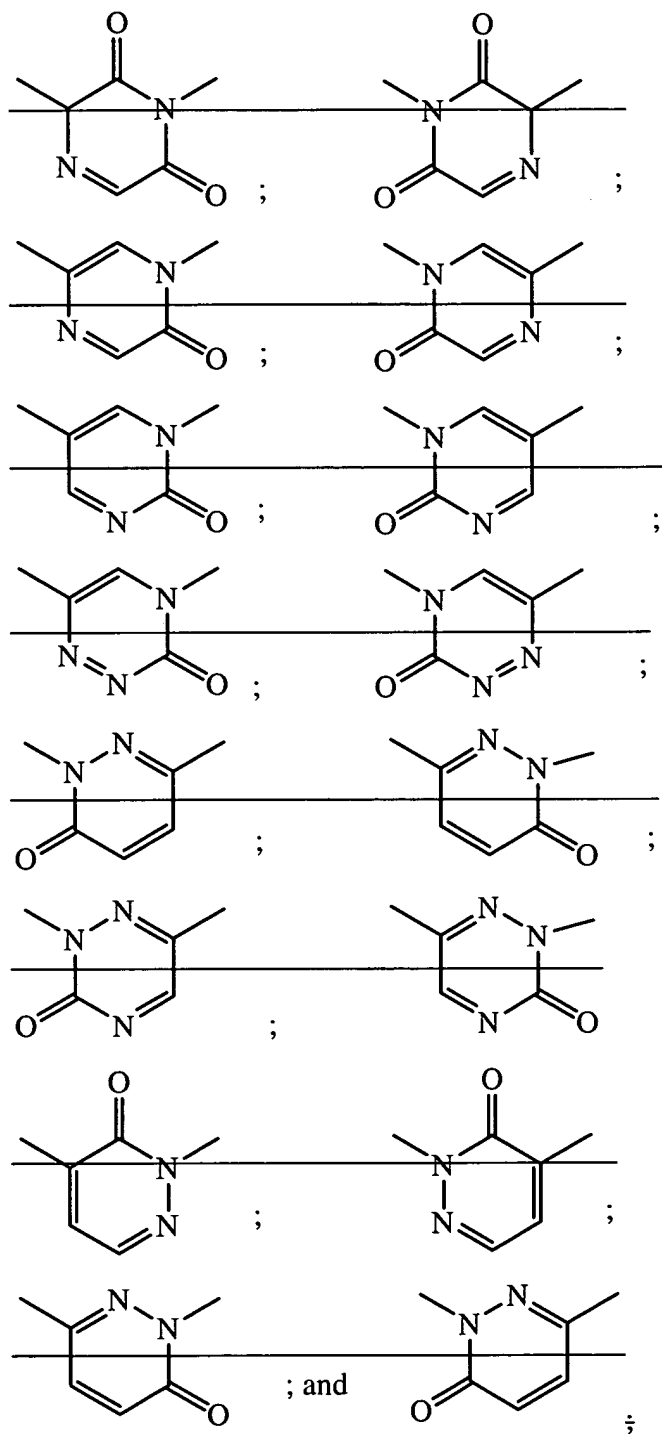
heterocycloalkyl; phenyl; benzyl; or 5- or 6-membered heteroaryl;

X is O, S, N(H), or N(C<sub>1</sub>-C<sub>6</sub> alkyl);

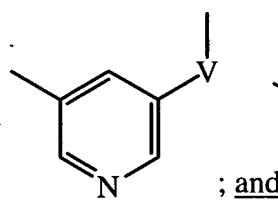
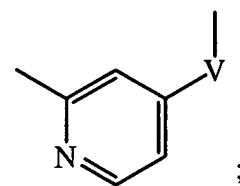
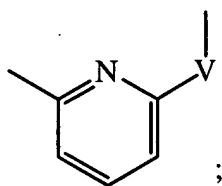
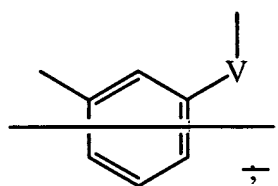
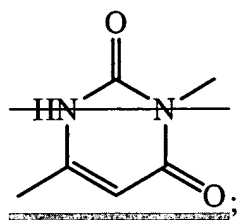
Each V is independently C(H) or N;

D is a cyclic diradical group selected from:

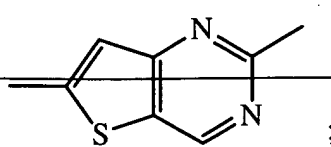
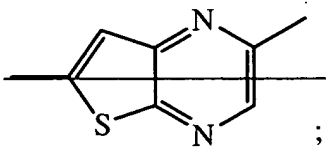
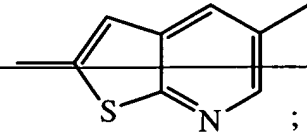
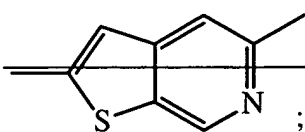
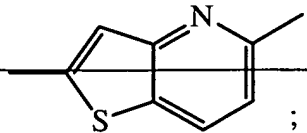
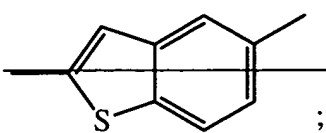
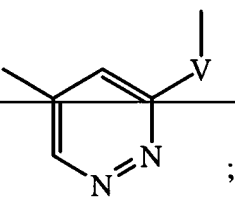
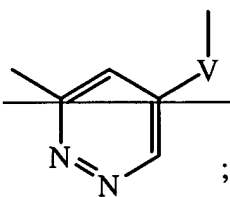
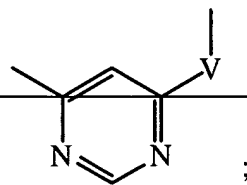
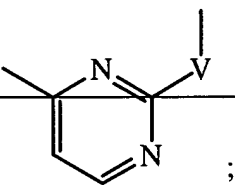
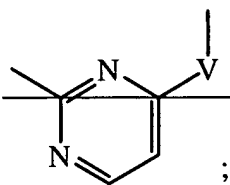
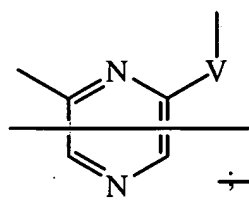
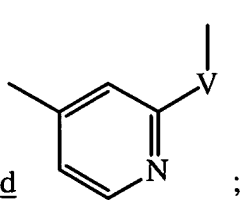


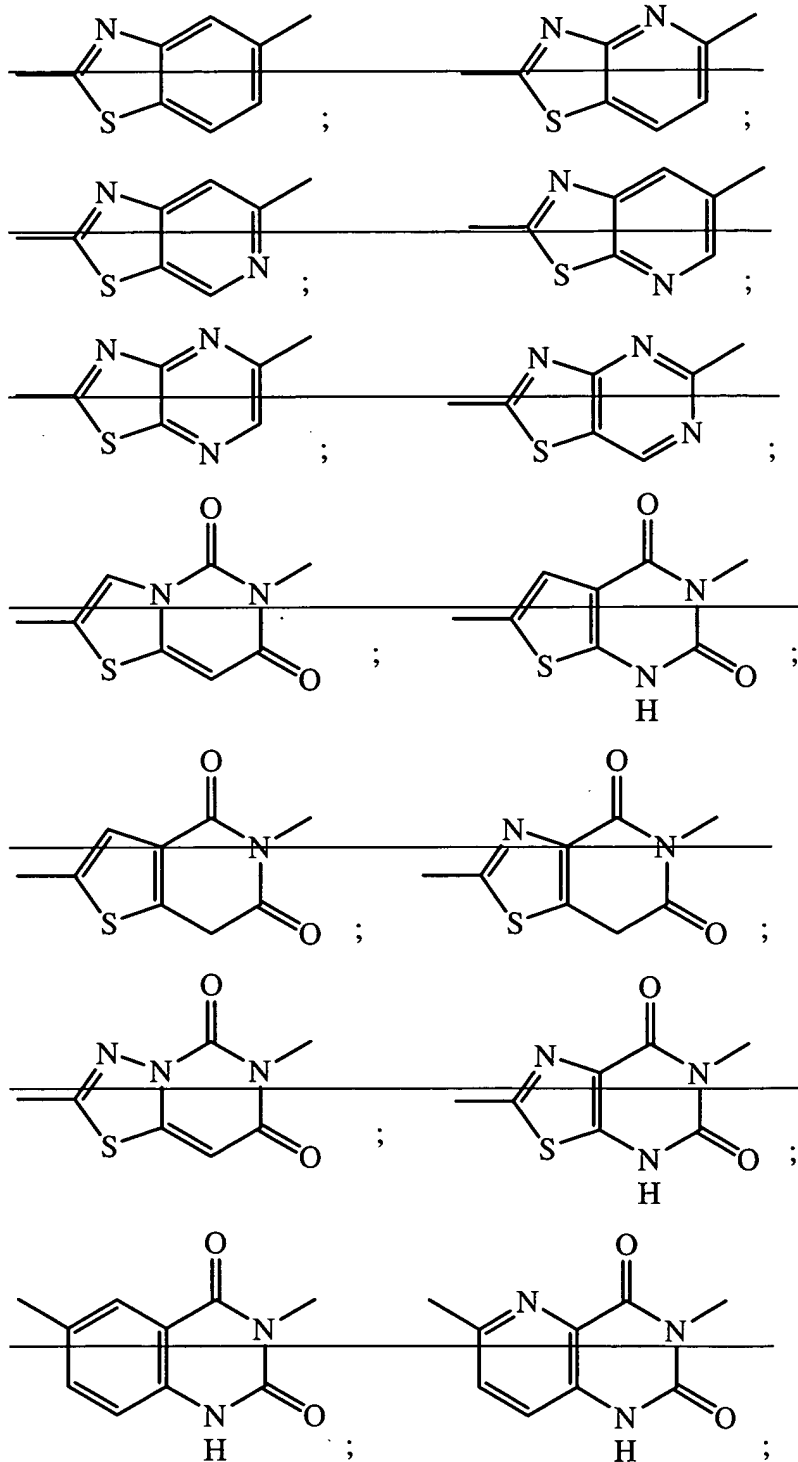


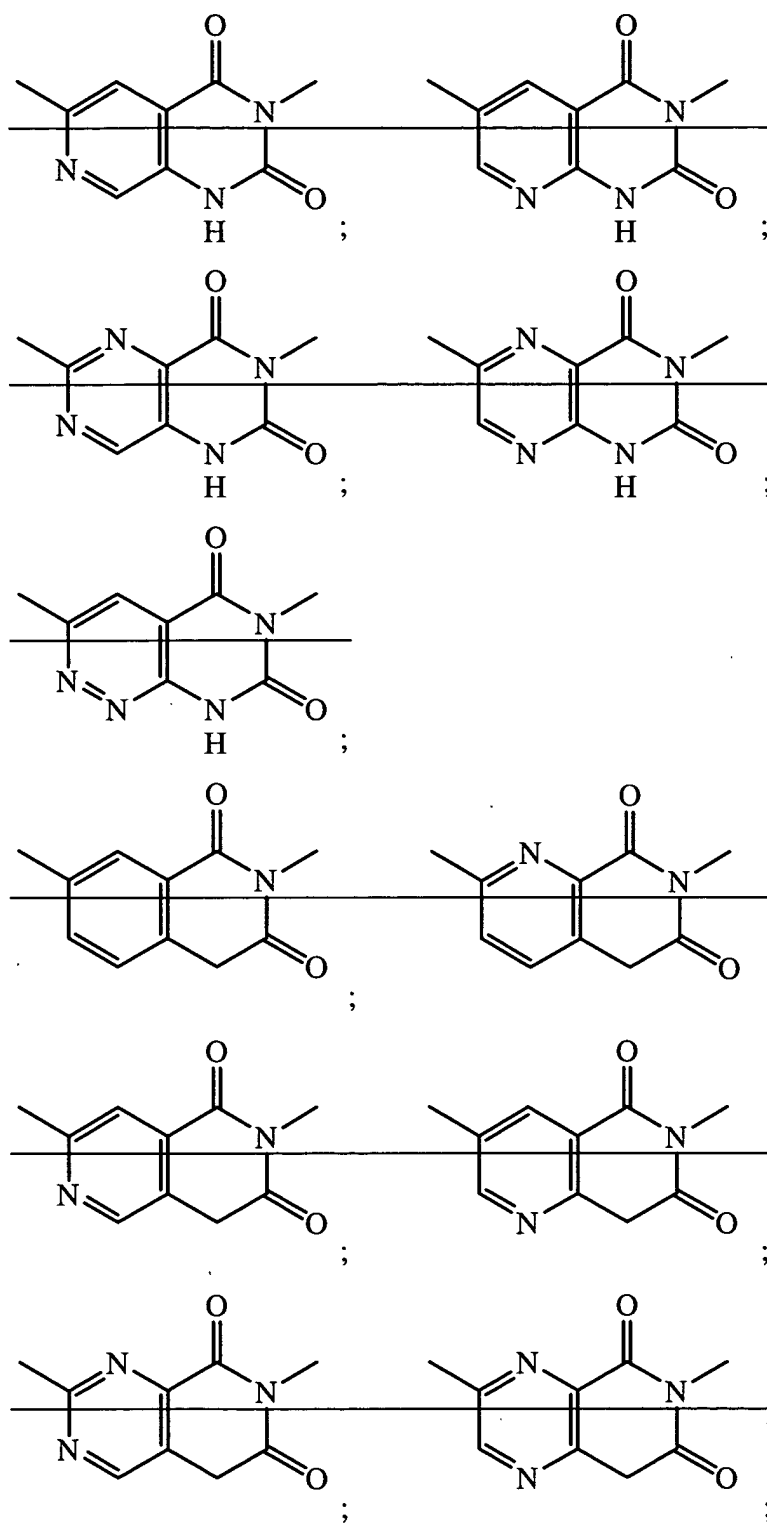


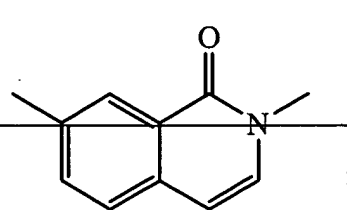
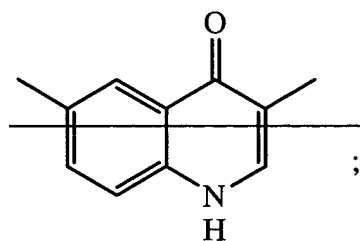
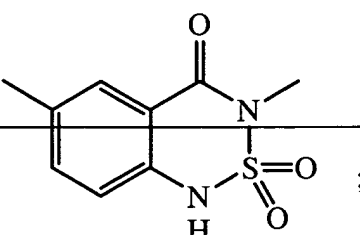
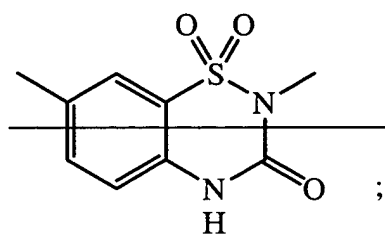
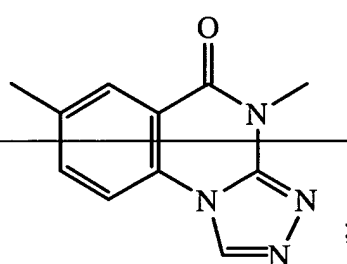
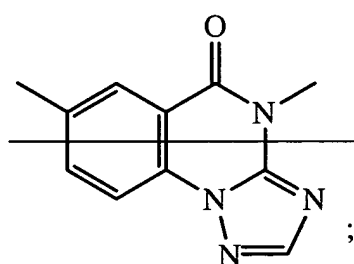
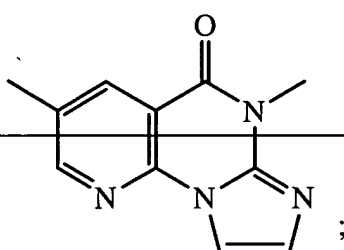
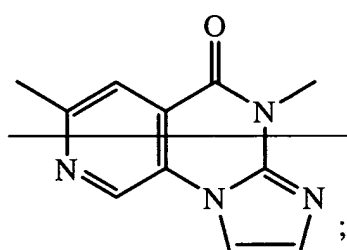
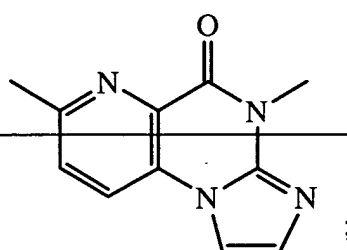
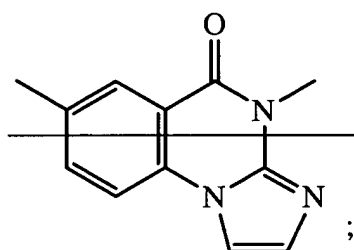
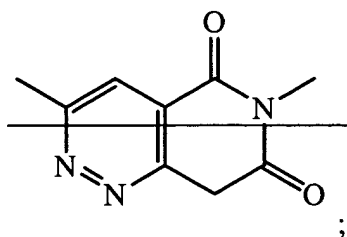


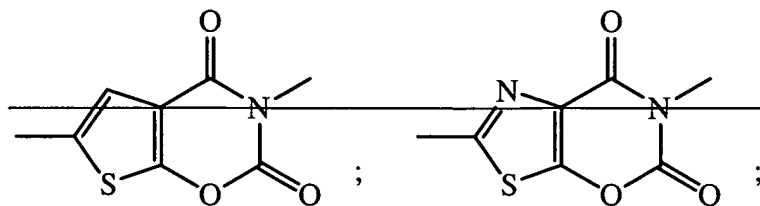
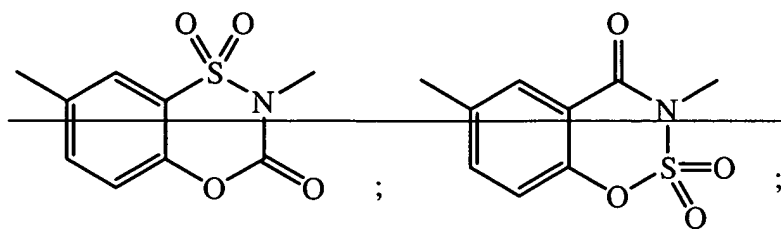
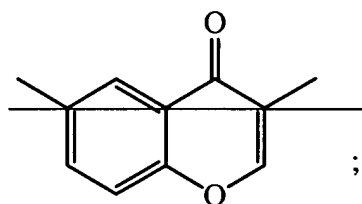
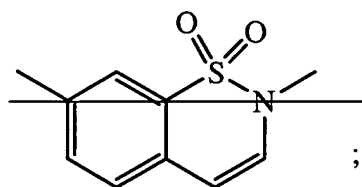
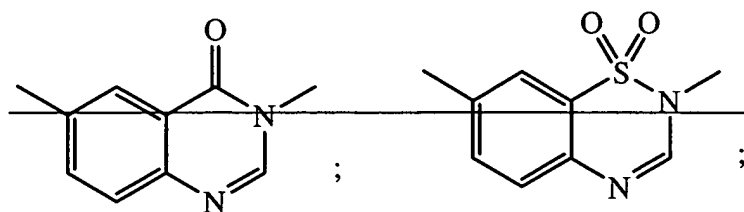
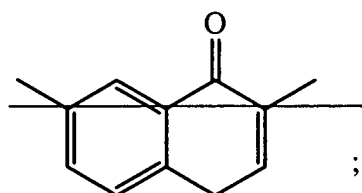
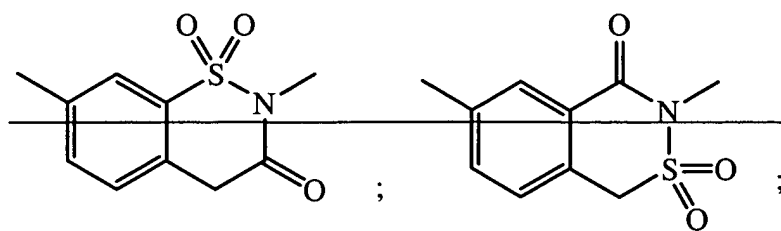
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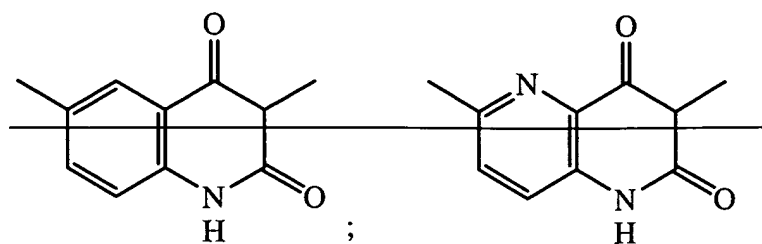
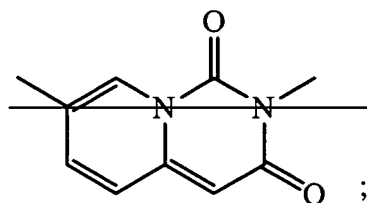
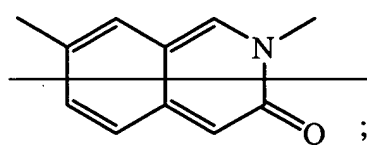
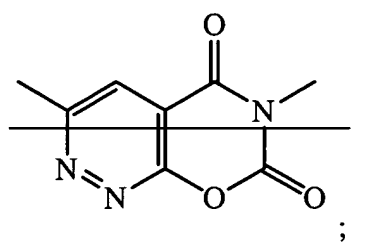
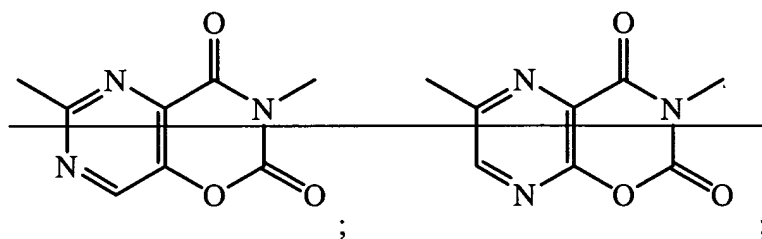
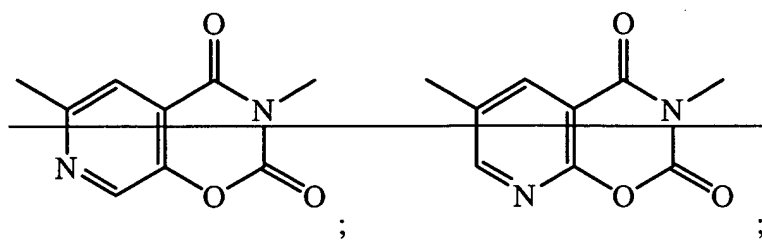
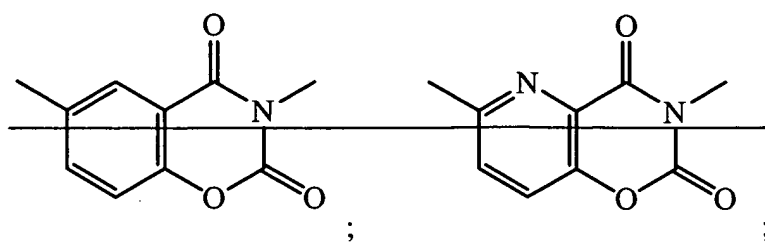


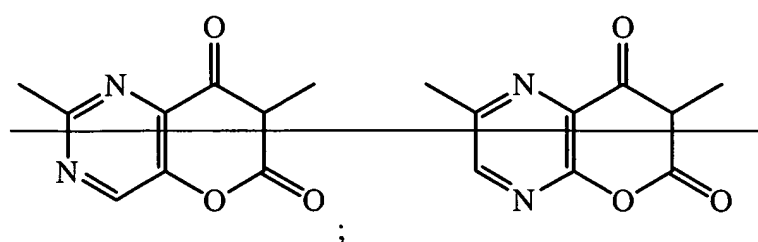
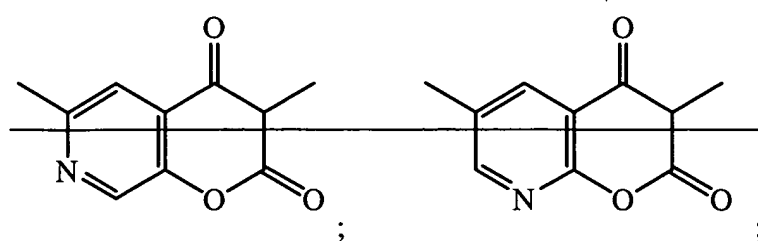
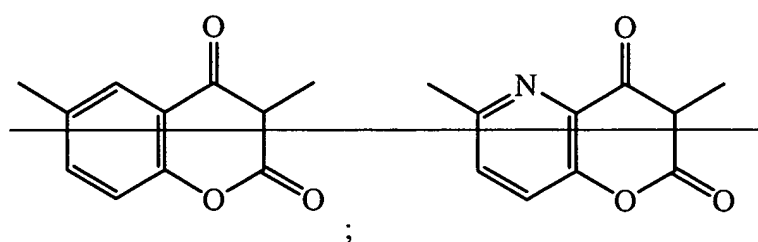
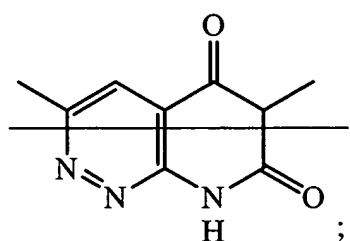
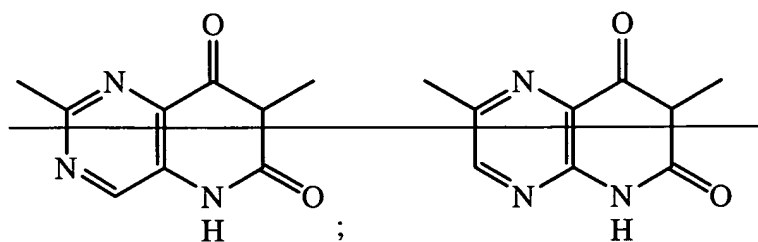
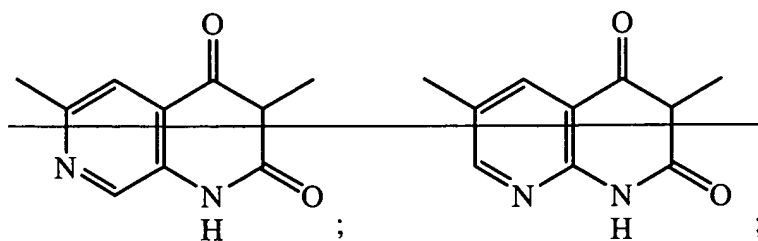


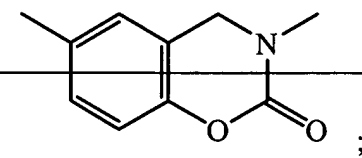
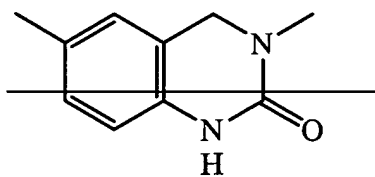
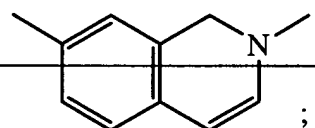
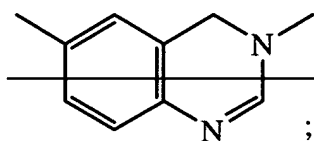
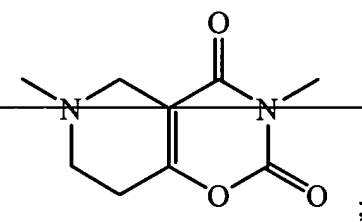
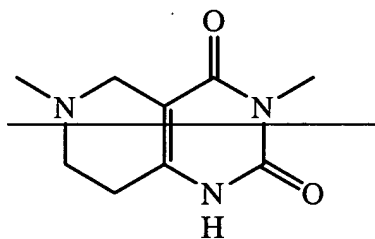
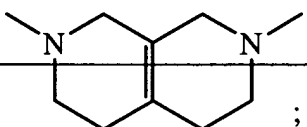
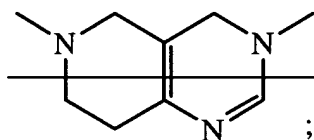
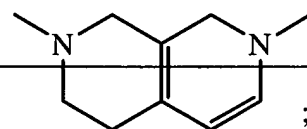
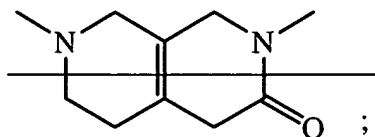
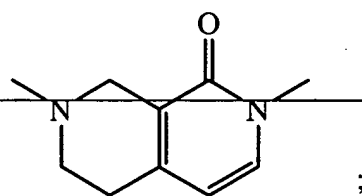
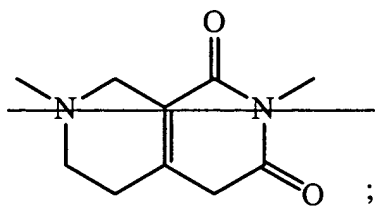
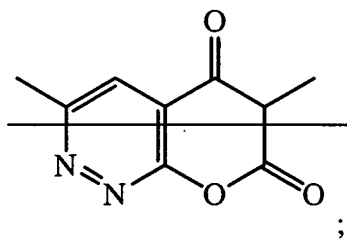




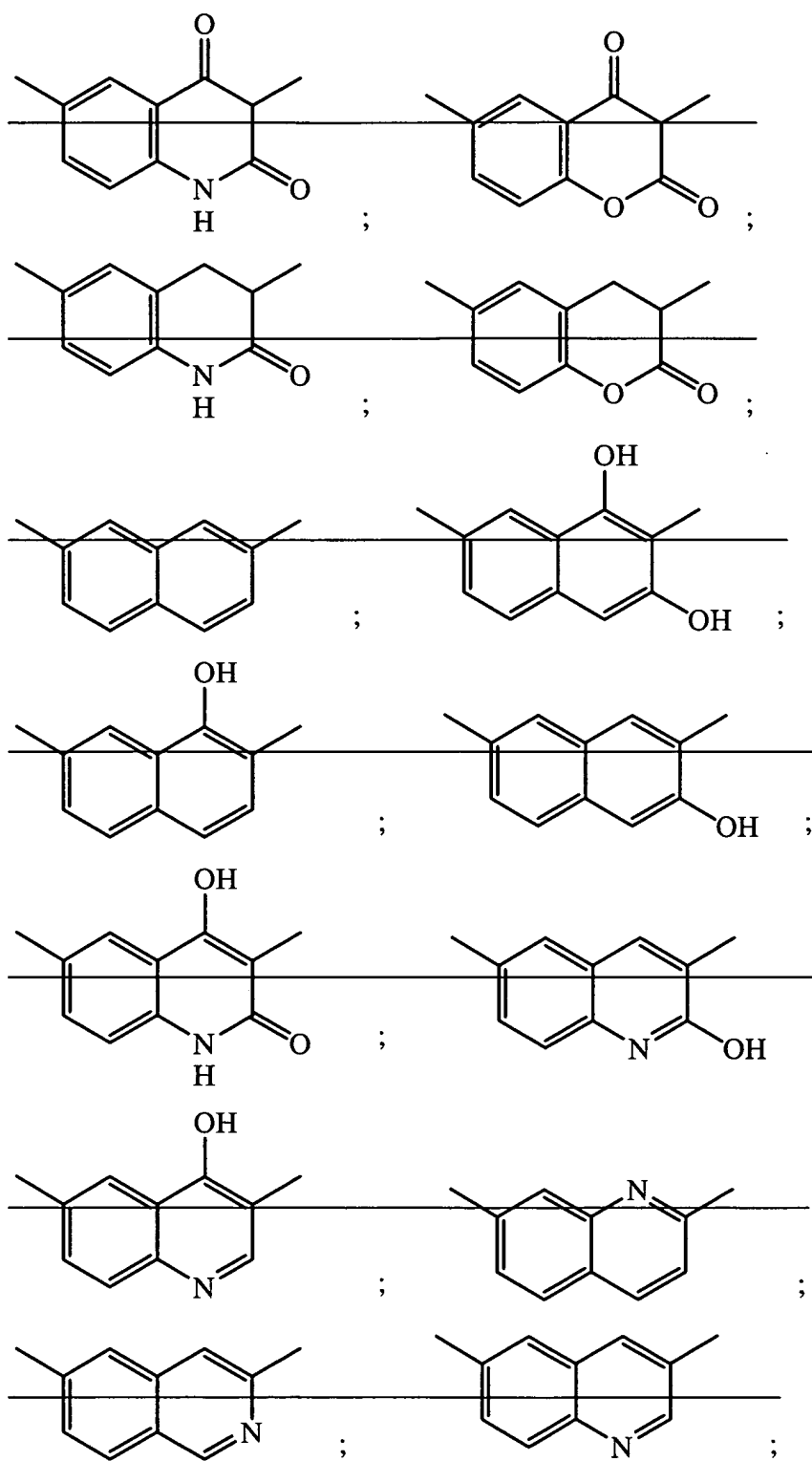


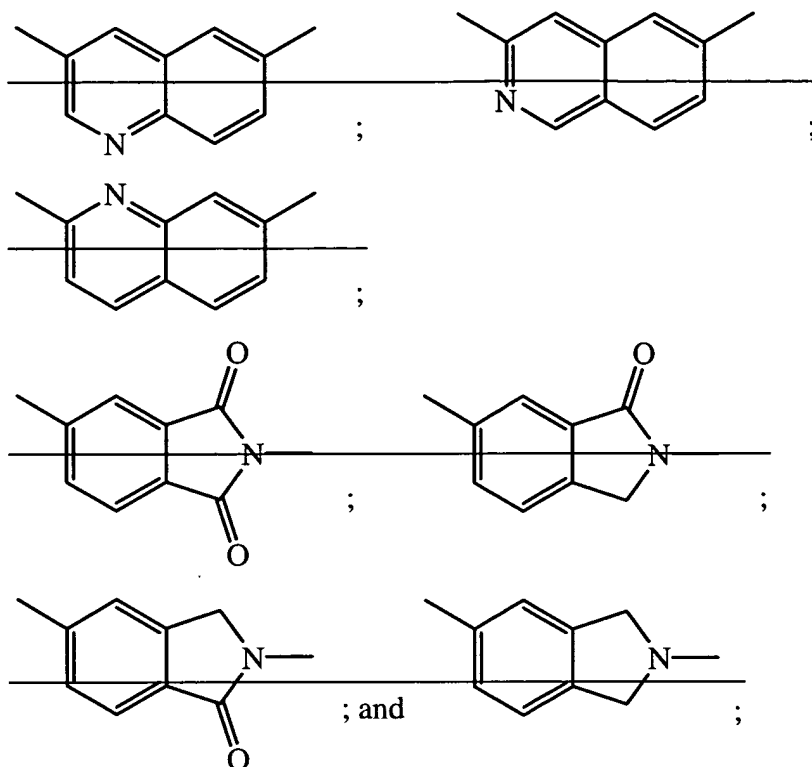












wherein the group D may be unsubstituted or substituted on a carbon atom or a nitrogen atom by replacement of a hydrogen atom with a group selected from:

CH<sub>3</sub>;

CF<sub>3</sub>;

C(O)H;

CN;

HO;

CH<sub>3</sub>O;

C(F)H<sub>2</sub>O;

C(H)F<sub>2</sub>O; and

CF<sub>3</sub>O;

wherein a carbon atom in the group D may further be substituted with F;

V<sup>1</sup> is a 5-membered heteroarylenyl containing carbon atoms and from 1 to 4 heteroatoms selected from 1 O, 1 S, 1 NH, 1 N(C<sub>1</sub>-C<sub>6</sub> alkyl), and 4 N, wherein the O and S atoms are not both present, and wherein the

heteroarylenyl may optionally be unsubstituted or substituted with 1 substituent selected from fluoro, methyl, hydroxy, trifluoromethyl, cyano, and acetyl;

wherein each C<sub>8</sub>-C<sub>10</sub> bicycloalkyl is a bicyclic carbocyclic ring that contains 8-, 9-, or 10-member carbon atoms which are 5,5-fused, 6,5-fused, or 6,6-fused bicyclic rings, respectively, and wherein the ring is saturated or optionally contains one carbon-carbon double bond;

wherein each 8- to 10-membered heterobicycloalkyl is a bicyclic ring that contains carbon atoms and from 1 to 4 heteroatoms independently selected from 2 O, 1 S, 1 S(O), 1 S(O)<sub>2</sub>, 1 N, 4 N(H), and 4 N(C<sub>1</sub>-C<sub>6</sub> alkyl), and wherein when two O atoms or one O atom and one S atom are present, the two O atoms or one O atom and one S atom are not bonded to each other, and wherein the ring is saturated or optionally contains one carbon-carbon or carbon-nitrogen double bond, and wherein the heterobicycloalkyl is a 5,5-fused, 6,5-fused, or 6,6-fused bicyclic ring, respectively,

wherein each heterocycloalkyl is a ring that contains carbon atoms and from 1 to 4 heteroatoms independently selected from 2 O, 1 S, 1 S(O), 1 S(O)<sub>2</sub>, 1 N, 4 N(H), and 4 N(C<sub>1</sub>-C<sub>6</sub> alkyl), and wherein when two O atoms or one O atom and one S atom are present, the two O atoms or one O atom and one S atom are not bonded to each other, and wherein the ring is saturated or optionally contains one carbon-carbon or carbon-nitrogen double bond;

wherein each heterocycloalkylenyl is a ring diradical that contains carbon atoms and from 1 to 3 heteroatoms independently selected from 1 O, 1 S, 1 S(O), 1 S(O)<sub>2</sub>, 1 N, 2 N(H), and 2 N(C<sub>1</sub>-C<sub>6</sub> alkyl), and wherein when one O atom and one S atom are present, the one O atom and one S atom are not bonded to each other, and wherein the ring is saturated or optionally contains one carbon-carbon or carbon-nitrogen double bond;

wherein each 5-membered heteroaryl contains carbon atoms and from 1 to 4 heteroatoms independently selected from 1 O, 1 S, 1 N(H), 1 N(C<sub>1</sub>-C<sub>6</sub> alkyl), and 4 N, and each 6-membered heteroaryl contains carbon atoms

and 1 or 2 heteroatoms independently selected from N, N(H), and N(C<sub>1</sub>-C<sub>6</sub> alkyl), and 5- and 6-membered heteroaryl are monocyclic rings;

wherein a 5-membered heteroarylenyl is a 5-membered monocyclic diradical ring that contains carbon atoms and from 1 to 4 heteroatoms independently selected from 1 O, 1 S, 1 N(H), 1 N(C<sub>1</sub>-C<sub>6</sub> alkyl), and 4 N, wherein the 1 O atom and 1 S atom are not both present, and 6-membered heteroarylenyl is a 6-membered monocyclic diradical ring that contains carbon atoms and 1 or 2 heteroatoms independently selected from 2 N;

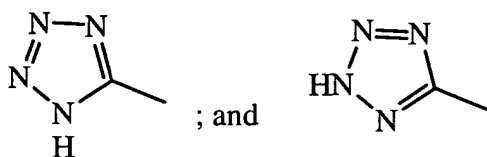
wherein each heterobiaryl contains carbon atoms and from 1 to 4 heteroatoms independently selected from 1 O, 1 S, 1 N(H), 1 N(C<sub>1</sub>-C<sub>6</sub> alkyl), and 4 N, and where the 8-, 9-, and 10-membered heterobiaryl are 5,5-fused, 6,5-fused, and 6,6-fused bicyclic rings, respectively, and wherein at least 1 of the 2 fused rings of a bicyclic ring is aromatic, and wherein when the O and S atoms both are present, the O and S atoms are not bonded to each other;

wherein with any (C<sub>1</sub>-C<sub>6</sub> alkyl)<sub>2</sub>-N group, the C<sub>1</sub>-C<sub>6</sub> alkyl groups may be optionally taken together with the nitrogen atom to which they are attached to form a 5- or 6-membered heterocycloalkyl; and

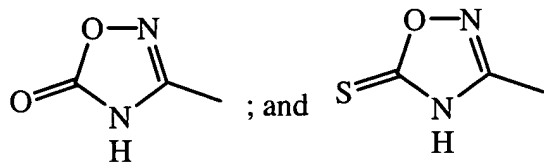
wherein each group and each substituent recited above is independently selected.

**Claim 2 (original).** The compound according to Claim 1, or a pharmaceutically acceptable salt thereof, wherein Z is HO<sub>2</sub>C.

**Claim 3 (original).** The compound according to Claim 1, or a pharmaceutically acceptable salt thereof, wherein Z is selected from:

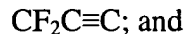
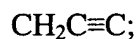


**Claim 4 (original).** The compound according to Claim 1, or a pharmaceutically acceptable salt thereof, wherein Z is selected from:



**Claim 5 (original).** The compound according to any one of Claims 1 to 4, or a pharmaceutically acceptable salt thereof, wherein Q is  $N(R^6)C(O)$ .

**Claim 6 (original).** The compound according to any one of Claims 1 to 4, or a pharmaceutically acceptable salt thereof, wherein Q is selected from:



**Claim 7 (canceled).**

**Claim 8 (original).** A pharmaceutical composition, comprising a compound according to Claim 1, or a pharmaceutically acceptable salt thereof, admixed with a pharmaceutically acceptable carrier, excipient, or diluent.

**Claim 9 (canceled).**

**Claim 10 (currently amended).** A method for treating osteoarthritis, comprising administering to a patient suffering from osteoarthritis ~~or rheumatoid arthritis~~ a nontoxic effective amount of a compound according to Claim 1, or a pharmaceutically acceptable salt thereof.

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Adam Richard Johnson

**Claim 11 (canceled).**